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Christine Todd Whitman, Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on the HPV Test Plan for the alkyl diphenyl oxide sulfonates (ADPODS) class of chemicals.

Dear Administrator Whitman:

The following comments on the Dow Chemical Company (Dow Chemical) High Production Volume (HPV) Chemicals Challenge Program test plan for the ADPODS class of chemicals are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

Dow Chemical submitted its test plan on December 20, 2002. Dow Chemical chose to give hazard information on five ADPODS chemicals included in the HPV Challenge Program, and to add two chemicals to their test plan, in order to strengthen their category approach in analyzing ADPODS chemicals. A list of their proposed chemicals, along with the Chemical Abstract Service (CAS) Registry number, is given below.

TSCA Chemical name	CAS #	
Benzene, 1,1'-oxybis-, sec-hexyl derivs., sulfonated, sodium salts	147732-60-3	*Not on HPV list
Benzenesulfonic acid, decyl(sulfophenoxy)-	70191-75-2	
Benzenesulfonic acid, decyl(sulfophenoxy)-, disodium salt	36445-71-3	
Benzene, 1,1'-oxybis-, sec-dodecyl derivs., sulfonated, sodium salts	149119-20-0	
Benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated	119345-03-8	
Benzene, 1,1'-oxybis-,tetrapropylene derivs., sulfonated, sodium salts	119345-04-9	
Benzenesulfonic acid, hexadecyl-(sulfophenoxy)-, disodium salt	65143-89-7	*Not on HPV list

The ADPODS chemicals consist of a basic diphenyl oxide structure, with one or two alkyl side chains and sulfonate group attachments. The alkyl groups range from C6 to C16 in size, and the sulfonate attachments can be either the acid or sodium salt. Each member of the

group functions as a bipolar anionic surfactant. This category complies with the EPA definition of a chemical category for the purposes of the HPV Chemical Challenge Program. Chemicals should have a common Structure-Activity Relationship, which creates a predictable pattern of environmental and human health effects, physiochemical properties and environmental fate. We agree with Dow Chemical regarding the use of one chemical category, and commend them for condensing this group of 150 plus chemicals into a group of seven, which can be further condensed by category analogy, thus minimizing the number of animals killed.

Dow Chemical presented a detailed description of the ADPODS chemicals, and conducted a thorough review of the scientific literature regarding chemical properties and toxicity data for the category. It also employed category analogy whenever possible to fulfill Screening Information Data Set (SIDS) endpoints as suggested by the EPA in the letter sent to HPV Challenge Program participants on October 14, 1999. In Appendix A of its test plan, Dow Chemical gave a summary of the physiochemical and toxicological data available, as well as whether tests were proposed, for each of the seven chemicals. There is a large body of evidence that suggests that the ADPODS chemicals have consistent profiles of mammalian toxicity, and a number of studies suggesting that they are not reproductively or developmentally toxic. Repeat dose studies show that the ADPODS are "low in systemic toxicity," (test plan p. 19) and have little or no genotoxic or tumorigenic properties. Studies also show "a lack of an effect on reproduction," (test plan p. 21). A developmental toxicity study was included in the reproductive data section, with "depression of maternal weight gain" seen but no "significant adverse effects at either dose," (test plan p. 21). Eleven subchronic and chronic tests across mammal species indicated, "in all instances, there were **no adverse effects in any of these** [reproductive] **organs,**" (test plan p. 21). Upon reviewing the robust summaries, we find that in those 11 repeat dose studies that looked at reproductive system endpoints, NOAELs ranged from 50-500 mg/kg bw/day. Organ weight, autopsy and histological examinations revealed no effects on reproductive organs or systems. All LOAELs, which ranged from 200-1223 mg/kg bw/day, were determined using effects on other organs, such as liver or kidney weight gain. It would seem that mammalian toxicity endpoints are largely fulfilled for this screening level program.

It is therefore surprising and extremely disappointing that Dow Chemical proposed OECD Test Guideline 422, Combined Repeat Dose/Repro/Developmental Screen, on CAS RN chemicals 147732-60-3 and 65143-89-7. These two chemicals are **not even listed as part of the EPA HPV Challenge Program list** (Test plan p. 7). While it is useful to include these chemicals to enrich the ADPODS category, it is irresponsible for Dow Chemical to propose the killing of at least 1,350 animals testing two chemicals that are not even part of the program.

As stated above and by Dow Chemical several times in their test plan, there is more than enough information to draw a preliminary conclusion that the ADPODS chemicals are not reproductively or developmentally toxic. Data is wide-ranging in both duration of investigation and species studied. It is unlikely that the screening program protocol OECD Test Guideline 422 will produce reproductive or developmental effects at a lower dose than those used in the comprehensive toxicity studies cited above. A screening-level program

such as HPV does not require further testing on such a data-rich group of chemicals. Per the aforementioned October 14, 1999 agreement letter, participants are instructed to "conduct a thoughtful, qualitative analysis," and not to use a "rote checklist approach." Yet by proposing OECD Test Guideline 422, this is precisely what Dow Chemical has done. Dow Chemical stated that there is a "true picture of repeated dose toxicity," (test plan p. 20), and that by completing OECD test Guideline 422 "additional data will be generated." This is contrary to the October 14, 1999 agreement. Manufacturers are required to "maximize the use of existing and scientifically adequate data to minimize further testing," but time and time again our organizations have brought to the EPA's attention the lack of motivation by participants to do so. We request that the EPA provide Dow Chemical with guidance regarding the October 1999 agreement letter. The unnecessary killing of over 1,300 animals could be prevented if the spirit of the HPV Chemical Challenge Program and the October 1999 agreement letter were to be followed.

I look forward to a prompt and favorable response to our concerns. I may be reached at 202-686-2210, ext. 335, or via email at *kstoick@pcrm.org.*

Sincerely,

Kristie Stoick, MPH
Research Analyst

Chad Sandusky,
Director of Research